

What is claimed is:

- 1 1. A method of analyzing tissue, the method comprising:
 - 2 illuminating a tissue with coherent light;
 - 3 receiving light reflected from the tissue at a detector to form a series of speckle
 - 4 patterns; and
 - 5 analyzing changes in the speckle patterns at time intervals sufficient to measure
 - 6 changes caused by Brownian motion of objects within the tissue.
- 1 2. The method of claim 1, further comprising compensating for extrinsic motion to
- 2 isolate the Brownian motion.
- 1 3. The method of claim 1, wherein the tissue is *in vivo*.
- 1 4. The method of claim 1, wherein the tissue is internal tissue.
- 1 5. The method of claim 4, wherein the illuminating step comprises providing an
- 2 invasive device coupled to a light source, passing the device into a patient, placing the device
- 3 in proximity to the tissue, and shining coherent light from the light source onto the tissue.
- 1 6. The method of claim 5, wherein the invasive device is selected from the group
- 2 consisting of a catheter, an endoscope, and a laparoscope.
- 1 7. The method of claim 5, wherein the placing step includes placing the device in
- 2 direct contact with the tissue.
- 1 8. The method of claim 5, wherein the invasive device comprises a catheter having a
- 2 first fiber that transmits light from the light source to the tissue, and a fiber array that receives
- 3 light remitted from the tissue.
- 1 9. The method of claim 1, wherein the coherent light comprises laser light.

1 10. The method of claim 1, wherein the speckle pattern is a far field image formed at
2 the detector.

1 11. The method of claim 1, wherein the analyzing step comprises comparing each of
2 the series of speckle patterns to a reference speckle pattern, and quantifying the differences
3 between each pattern and the reference pattern.

1 12. The method of claim 11, wherein the analyzing step comprises digitizing each of
2 the speckle patterns, and the quantifying step comprises evaluating a maximum cross-
3 correlation between each pattern and the reference pattern.

1 13. The method of claim 12, wherein the analyzing step further comprises
2 determining a decorrelation rate for the speckle patterns.

1 14. The method of claim 1, wherein the analyzing step further comprises analyzing
2 spatial characteristics of the speckle pattern to deduce structural characteristics of the tissue.

1 15. The method of claim 14, wherein the illuminating step comprises illuminating
2 multiple sections of the tissue in succession, the receiving step comprises forming a separate
3 series of speckle patterns for each respective section of the tissue, and the analyzing step
4 comprises analyzing each separate series of speckle patterns and comparing the separate
5 series to deduce structural differences between the respective sections of the tissue.

1 16. The method of claim 2, wherein compensating for extrinsic motion comprises
2 performing the receiving step during a diastole of a heartbeat.

1 17. The method of claim 2, wherein the receiving step comprises gathering reflected
2 light at a light receptor and transmitting the gathered light to the detector, and wherein
3 compensating for extrinsic motion includes coupling the receptor to the tissue.

1 18. The method of claim 2, wherein compensating for extrinsic motion includes
2 excluding changes in the speckle patterns caused by non-random motion during the analysis
3 step.

1 19. The method of claim 2, wherein extrinsic motion results from blood flow
2 between the tissue and the reflector, and the compensating step comprises replacing the blood
3 with a transparent solution.

1 20. The method of claim 1, wherein the tissue comprises atherosclerotic plaque.

1 21. A method of determining the susceptibility to rupture of an atherosclerotic plaque
2 having a lipid pool and a fibrous cap, the method comprising:
3 illuminating the plaque with coherent light;
4 receiving light reflected from the plaque at a detector to form a series of speckle
5 patterns;
6 gathering speckle pattern data at time intervals sufficient to measure Brownian
7 motion within the lipid pool; and
8 assessing the plaque's vulnerability to rupture from the amount of Brownian motion.

1 22. The method of claim 21, further comprising analyzing spatial characteristics of
2 the speckle pattern data to determine structural characteristics of the plaque.

1 23. The method of claim 22, wherein the analyzing step comprises assessing the
2 thickness of the fibrous cap.

1 24. The method of claim 23, wherein a plaque is considered vulnerable to rupture if
2 the thickness of the fibrous cap is less than about 60 microns.

1 25. The method of claim 22, wherein the analyzing step comprises assessing the
2 viscosity of the lipid pool.

1 26. The method of claim 25, wherein the plaque is considered vulnerable to rupture if
2 the viscosity of the lipid pool has a time constant of less than about 200 milliseconds.

1 27. The method of claim 25, wherein the plaque is considered likely to rupture if the
2 viscosity of the lipid pool has a time constant of less than about 100 milliseconds.

1 28. A method of detecting a vulnerable atherosclerotic plaque having a lipid pool and
2 a fibrous cap within a blood vessel, the method comprising:

3 illuminating a segment of the blood vessel *in vivo* with coherent light;
4 receiving light reflected from the interior vessel wall of the segment at a detector to
5 form a series of speckle patterns;
6 gathering speckle pattern data at time intervals sufficient to measure Brownian
7 motion within the interior vessel wall; and
8 comparing the speckle pattern data to a known speckle pattern for a normal blood
9 vessel and a known speckle pattern for an atherosclerotic plaque;
10 wherein speckle pattern data corresponding to a speckle pattern for an atherosclerotic
11 plaque indicates the segment of the blood vessel contains an atherosclerotic plaque.

1 29. The method of claim 28, further comprising analyzing spatial characteristics of
2 the speckle pattern data to determine structural characteristics of the plaque.

1 30. The method of claim 29, wherein the analyzing step comprises assessing the
2 thickness of the fibrous cap.

1 31. The method of claim 30, wherein a plaque is considered vulnerable to rupture if
2 the thickness of the fibrous cap is less than about 60 microns.

1 32. The method of claim 29, wherein the analyzing step comprises assessing the
2 viscosity of the lipid pool.

1 33. The method of claim 32, wherein the plaque is considered vulnerable to rupture if
2 the viscosity of the lipid pool has a time constant of less than about 200 milliseconds.

1 34. The method of claim 32, wherein the plaque is considered likely to rupture if the
2 viscosity of the lipid pool has a time constant of less than about 100 milliseconds.

1 35. A fiber optic probe for detecting speckle patterns in a sample, the probe
2 comprising
3 a catheter including a rotatable inner shaft and a transparent outer sheath;
4 a fiber array housed within the shaft and comprising a central optical fiber for
5 transmitting incident light to the sample and multiple optical fibers for transmitting light
6 remitted from the sample; and
7 a mirror arranged near a distal end of the shaft to reflect light passing through the
8 fiber array onto a sample outside the transparent outer sheath and back from the sample
9 through the fiber array.

1 36. The fiber optic probe of claim 35, wherein the shaft can rotate 360 degrees within
2 the sheath.

1 37. The fiber optic probe of claim 35, further comprising an inflatable balloon
2 connected to the sheath.

1 38. An optical system for detecting speckle patterns in a sample, the system
2 comprising
3 a fiber optic probe of claim 35;
4 a coherent light source connected to the central optical fiber within the fiber array;
5 a detector to receive light remitted from the sample; and
6 a processor to process the remitted light and to analyze speckle patterns remitted from
7 the sample.

1 **39. The system of claim 38, wherein the processor comprises a reference speckle**
2 **pattern.**

1 **40. The system of claim 38, wherein the processor comprises an analog-digital**
2 **converter to convert the analog remitted light into a digital signal.**